

RANCH HAND ADVISORY COMMITTEE MEETING
October 26-27, 1998

Holiday Inn Riverwalk, Tarantella Room #4
San Antonio, Texas

The meeting was called to order by chairperson Dr. Robert W. Harrison, University of Rochester at 1:04 p.m., October 26, 1998. Others present were: Dr. Turner Camp, Veterans of Foreign Wars, Dr. Irene Check, Northwestern University Medical School, Dr. Ronald Trewyn, Kansas State University and Dr. Michael Stoto, George Washington University.

Specialists and staff present were: Dr. Nancy Dalager, Dr. Mary Paxton, and Dr. Han Kang, Department of Veterans Affairs; Dr. Rebecca Klemm and Mr. John Boyle, DVA contractor representatives; LTC Julie Robinson, Chief of Population Research, Dr. Joel Michalek, Dr. Ed Martin, Mr. Ed Blancas, Mr. Richard Ogershok, Dr. Richard Albanese, and Dr. Jay Miner, Brooks Air Force Base; Bill Grubbs and Megan Yeager, Science Application International Corporation; Dr. Essam Enan and Dr. Fumio, Matsumura University of California/Davis; Dr. Philip Kern, Veterans Administration, Little Rock, AR; Clark Brooks, San Diego Union Tribune; Mr. Ronald Coene, Committee Executive Secretary; Ms. Barbara Jewell and Ms. Linda Vetsch, Committee Staff, National Center for Toxicological Research.

Mr. Coene pointed out the minutes of the last meeting in this meeting's binder; and reported that they had previously been distributed for mail ballot, and were approved by mail.

Dr. Harrison called for comments or changes to the published agenda. He requested each presenter to allow at least half their allotted time for questions and on-the-spot committee discussions instead of holding discussion to the end of the day as presently scheduled. There was no objection to that change.

ARMY CHEMICAL CORPS VIETNAM VETERANS HEALTH STUDY

Dr. Han Kang, study director for the Department of Veterans Affairs (VA), gave a brief review of the background on the congressionally mandated program and its study design. He noted that the Congress by P.L. 102-4, mandated an investigation of the current knowledge of the health effects of Agent Orange or other herbicides used by the U.S. military in Vietnam. It also asked them to make a number of research recommendations to fill gaps in the current knowledge. In July 1993, the National Academy of Sciences (NAS) issued their first report to VA and in the report NAS highly recommended that the VA follow up with additional studies.

This study is designed as a retrospective cohort study comparing the health experience of the Army Chemical Corps Vietnam veterans to the health of those who did not serve

in Vietnam but served in the Army Chemical Corps stateside. Their collection method included computer-assisted telephone interviews, medical records review, and a serum dioxin assessment to document that indeed Army Chemical Corps Vietnam veterans had a higher exposure to dioxin than the selected control group.

Dr. Kang gave additional details on the study population, the targeted study outcomes including incidence of cancer and other health outcomes such as pregnancies and birth defects; the two-phase study design (feasibility of locating veterans after 30 years and gaining their cooperation, and a full health-effects evaluation); information collection methods and data analysis protocols; challenges associated with participant self-reporting procedures compared to availability/use of official medical records; and the willingness of veterans to participate and authorize release of their medical records.

Questions from the committee focused on whether there were sufficient control groups. Dr. Trewyn referred back to the last committee meeting in 1995 and his recollection that one or two additional control groups were recommended at that time. Specifically recommended was a control group of Army personnel totally unassociated with the Vietnam experience. He asked if that recommendation had been incorporated into the study? Dr. Kang responded that the recommendation had been discussed in the February 1996 document.

Committee questions were also asked about what was perceived as ignoring mortality data. Dr. Kang said they were not ignoring mortality data, that it was a separate study using the same cohort. He said the people identified as having served in the Army Chemical Corps have been followed for mortality outcome and those who are living are being given health surveys, so no information was being lost.

Also questioned was the value of dioxin levels in the blood 30 years after the last possible military exposure, versus non-military environmental exposures that could have been incurred before and since that time. Included in this discussion among the committee was the lack of knowledge of the kinetics of dioxin disappearance. Drs. Harrison and Trewyn agreed that it might be wise to find out that information before blood serums are evaluated.

There was considerable discussion about the composition of study groups and controls, what constituted exposure to Agent Orange, and how or whether exposure to other herbicides and chemicals would contribute to or confound the study information. Dr. Stoto opined that this VA study did seem to be following the guidance of the NAS/IOM when it recommended goals for these studies to Congress.

Dr. Kang reported that the CDC had much historical data and spent \$65 million to study ground troops who were deployed in Vietnam and also ground troops who were not deployed in Vietnam and went through the same type of health examinations and the health survey, or target study. That information has been well documented by CDC, and defines the health status of non-Vietnam veterans who were not necessarily in the

Chemical Corps including their dioxin levels. CDC was not able to demonstrate that the dioxin level of ground troops in Vietnam were higher than the dioxin levels of the non-Vietnam veteran ground troops.

Dr. Rebecca Klemm presented detailed information on the study's data collection methods and results, including location methods and rates for the veterans and their offspring; participation rates; medical records retrieval; and blood drawing methods. Her overheads are appended to these minutes. Dr. Klemm provided details about search processes, sources of addresses and phone numbers, etc., and gave a summary of the location ability of the study. She noted that John Boyle would help with the discussion on finding the participants.

Mr. Boyle noted the greatest challenge to this study, compared to something like the Air Force baseline study of 18 years ago, is that it's being done by telephone. It's not being done in person which limits them in both location and in some of the procedures. He discussed techniques to encourage participation in the study; statistics about the number of calls required to finish the survey; issues that developed out of the Women's Veterans study; non-response bias; short one-page questionnaire; the reasons for refusals; the Army Chemical Corps Health Survey, etc.

Dr. Klemm continued with a detailed presentation on blood serum collection processes and medical records follow-up, including their success in going to public/private providers to get the records as they had done for the women. She continued with details about the last phase of the study, blood collections.

Questions from the committee on Dr. Klemm's and Mr. Boyle's presentation included a question on the timeline for the study. Dr. Klemm reported that the pilot study had taken about 12 months, based on their experience with the pilot study they've planned on 14 months for the full study.

Dr. Michalek asked about questions on maternal risk factors such as smoking and drinking. Dr. Klemm said those were included in the telephone interview instrument. In response to another question from Dr. Michalek, Drs. Klemm and Kang assured him they were using the CDC definition of "birth defect" for their study and use the ICD9 coding. They all discussed the problems associated with parent definitions/descriptions of birth defects versus medical reports when available, versus the accepted CDC definitions, etc. They noted that the medical records would be the "gold standard" for their data gathering although to date most of their data have been based on self-reports since the medical records take so long to obtain.

Dr. Stoto asked what size blood sample was drawn and Dr. Kang reported that 30 ml is taken. Dr. Klemm also discussed her random selection mechanism for identifying blood donors, which starts with a roll of the dice.

Other questions from the committee were for additional information on the statistics about refusals to donate blood samples, death statistics, paternal lifestyle habits, validity of the questionnaire responses from survey participants, military demographics and impact on the study (to be discussed in a later presentation), and whether Chemical Corps personnel were actually the ones doing the handling and ground spraying of Agent Orange? All questions were answered to their satisfaction and no lingering doubts were voiced. Dr. Dalager offered a copy of their mortality study to clarify those questions.

There was a brief committee discussion about the value to the study of drawing blood and whether any useful information can be gleaned from it. Dr. Trewyn especially expressed doubt over its value. No specific recommendation was made.

Dr. Harrison said he would like to better understand what the VA's equivalent of an IRB was, and how it was used in consideration for this study. (Not answered at this time).

Dr. Kang began this session with a lengthy and detailed review of the dioxin analyses section of their handouts covering such issues as parent population characteristics and dioxin exposure responses on questionnaires and statistics derived from them. The only questions during this time were for minute clarifications of data presented, and whether the questionnaire spoke about spraying "herbicides" or "Agent Orange" specifically. It was explained that there are questions clearly using both terms on the questionnaire. Questions were also raised about incidence reported of chloracne and cirrhosis of the liver and whether it could be attributed to spraying exposure or hepatitis and other liver diseases. Dr. Harrison questioned the success of interviewing minority veterans, he asked if they participated in comparable numbers and if there were minority interviewers who conducted the telephone interviews. Dr. Kang believed that the racial response rate was similar to the parent population and said that there were minority interviewers. He also noted that all interviewers were women because they seemed to elicit more cooperation over the phone from interviewees. Dr. Camp asked how the budgeting for this study was holding up and Dr. Kang explained that the budget had been programmed by Congress to VA in 1995 so that the money is already allocated to proceed with the main 30-month full study. He noted that a major change in the study design would change the budget, but it's covered for now to carry through the full study.

Dr. Harrison announced the public session at 4:05 p.m. Clark Brooks, news reporter from the San Diego Union Tribune, asked several questions about who would be doing the Army "Corps of Engineers" (sic) study? Dr. Harrison said the VA. Mr. Brooks asked if the main VA study had not been approved as yet, and Dr. Kang and Dr. Harrison explained the purpose of this report on the results of the preliminary study and its impact on the main study. Mr. Brooks also questioned in what year the Ranch Hand Advisory Committee was constituted as opposed to the Agent Orange Working Group. Mr. Coene checked the charter and determined it was January 1981. He and Dr.

Harrison and Mr. Miner (former PI for the Air Force Health Study) gave some timeline details. That concluded the public questions and public session.

Dr. Kang continued with information requested earlier by the chairman on the use of IRB's (Institutional Review Board) for these studies. He noted that the IRB approvals for the health interview instrument (VA Washington, DC, IRB) and the blood drawing (reviewed several times and approved by the IRB each time) were separate.

At this point, Dr. Harrison asked Dr. Kang if he could frame a question that he would like this committee to answer about the VA study? Dr. Kang said, "Given the results of the field interview study that we have presented to you, is it the committee's opinion that we can proceed with our main study?" This induced a considerable discussion among the committee members (with Dr. Kang providing details) about the understood purpose of this study, the scientific versus political implications of the study to date, and the usefulness of expected future data to the mandate from Congress.

Dr. Harrison then asked, "Do we agree that, as it's presently constituted, that the study is feasible." The members responded in the affirmative.

Recommendations to the study: Add another control group (in addition to control group already included in the study) that is a totally clean, unexposed, military, non-spraying group. After considerable discussion, this was reported out as a minority opinion.

After discussions about setting the date for the next committee meeting, and the availability and review process for upcoming reports, it was projected that the next meeting would be in about six months, in the spring of 1999. No definite date was established.

The session adjourned at 4:47 p.m.

The Committee meeting continued in the same location on October 27, 1998, being called to order by Chairperson Harrison at 8:30 a.m.

AIR FORCE HEALTH STUDY

LTC Julie Robinson of Brooks Air Force Base introduced the discussion of this study on October 28, noting that the Mr. Richard Ogershok, program manager, and Dr. Joel Michalek, chief principal investigator, would be the primary presenters. She reviewed the history of the study noting that the Ranch Hand Epidemiologic Study deals with those individuals who were in Vietnam between 1962 and 1971 and flew aircraft spraying herbicides. That was the first time in U.S. military history that herbicides were used during warfare for both defensive and offensive measures. The agent of concern is Agent Orange but there were a variety of other agents also used in Vietnam, but Agent Orange was the agent that was responsible for dispersal of about 96% of the compound of concern, dioxin. The study goal is to see whether or not the Ranch Handers are experiencing any adverse health outcomes as a result of those occupational exposures. This is the 15th year of the health study and it's looking prospectively at each participant's health. She reviewed the infrastructure of the program at Brooks AFB.

Mr. Ogershok using overheads discussed the program management aspects of the Ranch Hand study. He noted that they consider the payoff for this program is that they provide a scientific basis for legislative action and they are a national resource for immunologic research.

Dr. Michalek gave a technical overview of the study from 1977 to date, going through slides with detailed comments on each. LTC Robinson then reviewed Cycle 5 of the study so that the rationale for progressing into Cycle 6 could be better understood.

The committee discussed with Dr. Michalek the timeline for receiving the Cycle 5 reports and what the review expectations were of the committee; how they could be most helpful in their review of the document. After considerable discussion, the consensus was that the Air Force would provide chapters through "pulmonary" for committee review at a meeting in April 1999 and review the rest in September 1999 (meetings in DC probably). In addition, the VA Army Chemical Corps study would provide an interim report on their current work at the September meeting. That schedule was agreed to with the understanding that the Executive Secretary would not know about a budget for FY 99 until a few weeks hence and those meeting plans might have to change. The committee agreed to that also.

After the break, Dr. Michalek continued with discussions of the latest findings, pointing out significant factors on each slide.

Dr. Essam Enan and Dr. Fumio Matsamura then spoke on the motivation for the measurements included in the study, and provided detailed comments on the

parameters of the study design for the TCDD half-life and adipose tissue analysis studies. Committee questions on these sessions dealt with specific questions about presentation statements and all were answered to the satisfaction of the questioner.

After lunch, Dr. Michalek introduced Dr. Philip Kern who spoke about the possibilities of the Air Force funding a cohort insulin resistance (glucose clamp) study based on the data collected at the Vertac plant in Jacksonville, Arkansas. After his presentation and detailed questions from the committee, Dr. Kern asked that the committee's recommendation be included in the minutes of this meeting. As stated by Dr. Harrison, "Well, certainly, the committee was not opposed."

Dr. Michalek next discussed the final special study on multiple analytes. He also spoke briefly about the fact that Clark Brooks was planning to write a supplement section on the Ranch Hand study for his newspaper. He noted they had had numerous correspondence and phone interviews to prepare him to write the article and that also was Mr. Brooks' reason for being at this meeting.

In addition, Dr. Michalek made extensive comments about incidences of possible perceived management interference in the design and conduct of this Ranch Hand study. He strongly stated that during the term of his association with the study since 1985 his decisions relative to the study and its structure had never been influenced by anyone or anything except recommendations for scientific excellence. He also introduced Dr. Albanese, a member of the study team before 1985, who spoke on issues during his term as principal investigator. This all generated a committee discussion on the committee's oversight and advisory responsibilities and the differences in perceived value of the Ranch Hand study to science. In this context, Dr. J. Miner stated for the record, "from 1985 until 1995 when I was involved with the study, I was Dr. Michalek's supervisor, there never was any command influence." Dr. Albanese also made short comments about a publication just last year that the Air Force refused to let him submit for publication with the National Academy of Sciences although it was published in another journal. That evoked concern from Dr. Harrison, but was not probed in depth.

The committee agreed to the position that the interpretation of the Air Force Health Study data should be uncolored by anyone's preconceptions, be they their own personal preconceptions, or those of the Executive Branch, or those of the Air Force superiors, and the study should be subject to the highest contemporary standards of scientific discourse.

Dr. Michalek next talked about plans for the study sixth cycle and LTC Robinson spoke briefly about the status of scanning and records maintenance and the increase in capabilities and contents since the last committee meeting. She also discussed the archive of biological samples and Dr. Michalek noted that they had a bank of 51,000 samples that could be available for other experimental work. The NAS has not

responded to their offer and he solicited ideas from the committee on uses for the samples, noting that the useful life of the samples is slipping away.

He then reported on plans for release of the 1984 preliminary birth defect report and the status of public release of data, especially related to an information request from Patrick Burton. The committee decided, based on Dr. Michalek's description, that the decision to release participant health information is the responsibility of the appropriate IRB's, not this advisory committee and the committee agrees with Dr. Michalek in his handling of Mr. Burton. The chairman also recommended that Dr. Michalek obtain a copy of the referee's critique of Burton's paper to help ascertain the basis for requesting potentially confidential study information.

After closing comments and some clarifications of comments made during the meeting, it was adjourned at 2:30 p.m.

Robert W. Harrison, M.D.
Chair, Ranch Hand Advisory Committee

Date

Ronald F. Coene, P.E.
Executive Secretary

Date

NOTE: Copies of the audio visuals used by the VA and the AF referenced in these minutes are available from the Executive Secretariat.

Meeting Handouts:

Veterans Affairs Overheads
Air Force Statement of Work